

# GLAD package: Gain and Loss Analysis of DNA

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# 1 Overview

This document presents an overview of the GLAD package (Gain and Loss Analysis of DNA). This package is devoted to the analysis of Array Comparative Genomic Hybridization (array CGH) (Pinkel et al., 1998; Snijders et al., 2001; Solinas-Toldo et al., 1997; Ishkanian et al., 2004). The methodology for detecting the breakpoints delimiting altered regions in genomic patterns and assigning a status (normal, gained or lost) to each chromosomal region described in the paper Hupé et al. (2004) is implemented in this package. Some graphical functions are provided as well.

## 2 Data

### 2.1 Public data set

We used the public data set described in Snijders et al. (2001). The data corresponds to 15 human cell strains with known karyotypes (12 fibroblast cell strains, 2 chorionic villus cell strains, 1 lymphoblast cell strain) from the NIGMS Human Genetics Cell Repository (<http://locus.umdj.edu/nigms>). Each cell strain has been hybridized on CGH arrays of 2276 BACs, spotted in triplicates. Two array CGH profiles from the data obtained by Veltman et al. (2003) are available.

### 2.2 Bladder cancer data

Bladder cancer data from tumors collected at Henri Mondor Hospital (CrÃ©teil, France) (Billerey et al., 2001) have been hybridized on CGH arrays composed of 2464 BACs (Radvanyi, Pinkel et al., unpublished results). In this data, only the log-ratios are provided and no information about clones is available since the data is not yet published. This data allows only some graphical functionalities to be shown and will be used as a support to illustrate some functions for array normalization (not yet available in the current version of the package).

## 3 GLAD classes

### 3.1 arrayCGH

This class stores raw values after images analysis. The object arrayCGH is a list with at least a data.frame named arrayValues and a vector named arrayDesign. The data.frame arrayValues must contain the following fields:

**Col** Vector of columns coordinates.

**Row** Vector of rows coordinates.

... Other elements can be added.

The vector arrayDesign is composed of 4 values: c(arrayCol, arrayRow, SpotCol, SpotRow). The array CGH is represented by arrayRow\*arrayCol blocs and each bloc is composed of SpotRow\*SpotCol spots. N.B.: Col takes the values in 1:arrayRow\*SpotRow and Row takes the values in 1:arrayCol\*SpotCol

### 3.2 profileCGH and profileChr

This class stores synthetic values related to each clone available on the arrayCGH. The object profileChr corresponds to data of only one chromosome. Objects profileCGH and profileChr are composed of a list with the first element profileValues which is a data.frame with the following columns names:

**LogRatio** Test over Reference log-ratio.

**PosOrder** The rank position of each clone on the genome.

**PosBase** The base position of each clone on the genome.

**Chromosome** Chromosome name.

**Clone** The name of the corresponding clone.

... Other elements can be added.

LogRatio, Chromosome and PosOrder are compulsory.

To create those objects you can use the function *as.profileCGH*.

## 4 Analysis of array CGH profile

Two functions are available: *glad* and *daglad*. The second one is an improvement of the first one which was originally described in Hupé et al. (2004). We recommend to use the *daglad* function. For fast computation use the option *smoothfunc=haarseg*.

### 4.1 Segmentation algorithms

Two algorithms are available for data segmentation:

- AWS (Polzehl and Spokoyny, 2000, 2002)
- HaarSeg (Ben-Yaacov and Eldar, 2008)

### 4.2 The *glad* function

A result of the GLAD methodology on cell line gm13330 (Snijders et al., 2001) is presented in **Figure 1**.

```
[1] ""
[1] "Have fun with GLAD"
[1] "For smoothing it is possible to use either"
[1] "the AWS algorithm (Polzehl and Spokoyny, 2002)"
[1] "or the HaarSeg algorithm (Ben-Yaacov and Eldar, Bioinformatics, 2008)"
[1] ""
[1] "If you use the package with AWS, please cite:"
[1] "Hupe et al. (Bioinformatics, 2004) and Polzehl and Spokoyny (2002)"
[1] ""
[1] "If you use the package with HaarSeg, please cite:"
[1] "Hupe et al. (Bioinformatics, 2004) and (Ben-Yaacov and Eldar, Bioinformatics, 2008)"
[1] ""
[1] "For fast computation it is recommended to use"
[1] "the daglad function with smoothfunc=haarseg"
[1] ""

> data(snijders)
> profileCGH <- as.profileCGH(gm13330)
> res <- glad(profileCGH, mediancenter = FALSE, smoothfunc = "lawsglad",
```

```

+     bandwidth = 10, round = 1.5, model = "Gaussian", lkern = "Exponential",
+     qlambda = 0.999, base = FALSE, lambdabreak = 8, lambdacluster = 8,
+     lambdaclusterGen = 40, type = "tricubic", param = c(d = 6),
+     alpha = 0.001, msize = 5, method = "centroid", nmax = 8,
+     verbose = FALSE)

[1] "Smoothing for each Chromosome"
[1] "Optimization of the Breakpoints"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005941868 secs
[1] "hclustglad"
      user system elapsed
0.004   0.000   0.001
[1] "clusterglad"
      user system elapsed
0.028   0.000   0.031
[1] "merge"
      user system elapsed
0       0       0
[1] "Temps findCluster: 0.207421064376831"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005304813 secs
[1] "Temps findCluster: 0.0502231121063232"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005249023 secs
[1] "Temps findCluster: 0.0496759414672852"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005671024 secs
[1] "hclustglad"
      user system elapsed
0       0       0
[1] "clusterglad"
      user system elapsed
0.028   0.000   0.028
[1] "merge"
      user system elapsed
0       0       0
[1] "Temps findCluster: 0.204145193099976"

```

```

[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005254984 secs
[1] "Temps findCluster: 0.0505199432373047"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005397081 secs
[1] "Temps findCluster: 0.0492150783538818"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.00527215 secs
[1] "Temps findCluster: 0.0505740642547607"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005265236 secs
[1] "Temps findCluster: 0.0491402149200439"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005267143 secs
[1] "Temps findCluster: 0.0503311157226562"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005250931 secs
[1] "Temps findCluster: 0.0496690273284912"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005245924 secs
[1] "Temps findCluster: 0.0505800247192383"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005395174 secs
[1] "Temps findCluster: 0.0493149757385254"
[1] "subsetdata"
      user system elapsed

```

```

0.000 0.000 0.001
[1] "diff"
Time difference of 0.005227089 secs
[1] "Temps findCluster: 0.0503919124603271"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.005231142 secs
[1] "Temps findCluster: 0.0491509437561035"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.005236149 secs
[1] "Temps findCluster: 0.0504119396209717"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.005244017 secs
[1] "Temps findCluster: 0.04905104637146"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.005252123 secs
[1] "Temps findCluster: 0.0502791404724121"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.00523591 secs
[1] "Temps findCluster: 0.0490140914916992"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.00522685 secs
[1] "Temps findCluster: 0.0502190589904785"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.005399942 secs
[1] "Temps findCluster: 0.0500178337097168"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.001
[1] "diff"

```

```

Time difference of 0.005243063 secs
[1] "Temps findCluster: 0.0505568981170654"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005415916 secs
[1] "Temps findCluster: 0.0488500595092773"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005240917 secs
[1] "Temps findCluster: 0.0502979755401611"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.002
[1] "diff"
Time difference of 0.01135302 secs
[1] "hclustglad"
      user system elapsed
0.000   0.000   0.001
[1] "clusterglad"
      user system elapsed
0.188   0.000   0.187
[1] "merge"
      user system elapsed
0.000   0.000   0.001
[1] "zone"
      user system elapsed
0.004   0.000   0.002
[1] "Temps findCluster: 0.419609069824219"
[1] "Results Preparation"

```

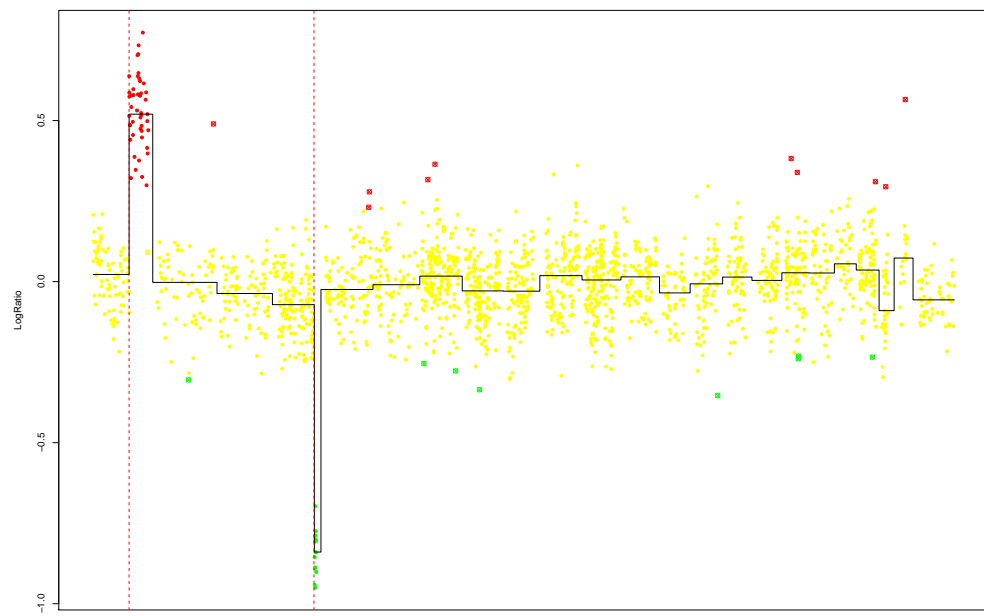


Figure 1: Results of glad on cell line gm13330 (Snijders data).



### 4.3 The *daglad* function

The algorithm implemented in this function is a slightly modified version of the GLAD algorithm.

```
> data(veltmann)
> profileCGH <- as.profileCGH(P9)
> profileCGH <- daglad(profileCGH, mediancenter = FALSE, normalrefcenter = FALSE,
+   genomestep = FALSE, smoothfunc = "lawsglad", lkern = "Exponential",
+   model = "Gaussian", qlambda = 0.999, bandwidth = 10, base = FALSE,
+   round = 1.5, lambdabreak = 8, lambdaclusterGen = 40, param = c(d = 6),
+   alpha = 0.001, msize = 5, method = "centroid", nmin = 1,
+   nmax = 8, amplicon = 1, deletion = -5, deltaN = 0.2, forceGL = c(-0.3,
+   0.3), nbsigma = 3, MinBkpWeight = 0.35, CheckBkpPos = TRUE)

[1] "Smoothing for each Chromosome"
[1] "Optimization of the Breakpoints"
[1] "DNA copy number calling"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.002
[1] "diff"
Time difference of 0.008697033 secs
[1] "hclustglad"
      user system elapsed
0         0         0
[1] "clusterglad"
      user system elapsed
0.188   0.000   0.186
[1] "merge"
      user system elapsed
0         0         0
[1] "zone"
      user system elapsed
0.004   0.000   0.002
[1] "Temps findCluster: 0.435307025909424"
[1] "jointure BkpInfo"
      user system elapsed
0.004   0.000   0.005
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.008485079 secs
[1] "hclustglad"
      user system elapsed
0         0         0
[1] "clusterglad"
      user system elapsed
0         0         0
[1] "merge"
      user system elapsed
```

```

0      0      0
[1] "zone"
      user system elapsed
0.000  0.000   0.001
[1] "Temps findCluster: 0.237226963043213"
[1] "jointure BkpInfo"
      user system elapsed
0.004  0.000   0.006
[1] "Check Breakpoints Position"
[1] "Results Preparation"

```

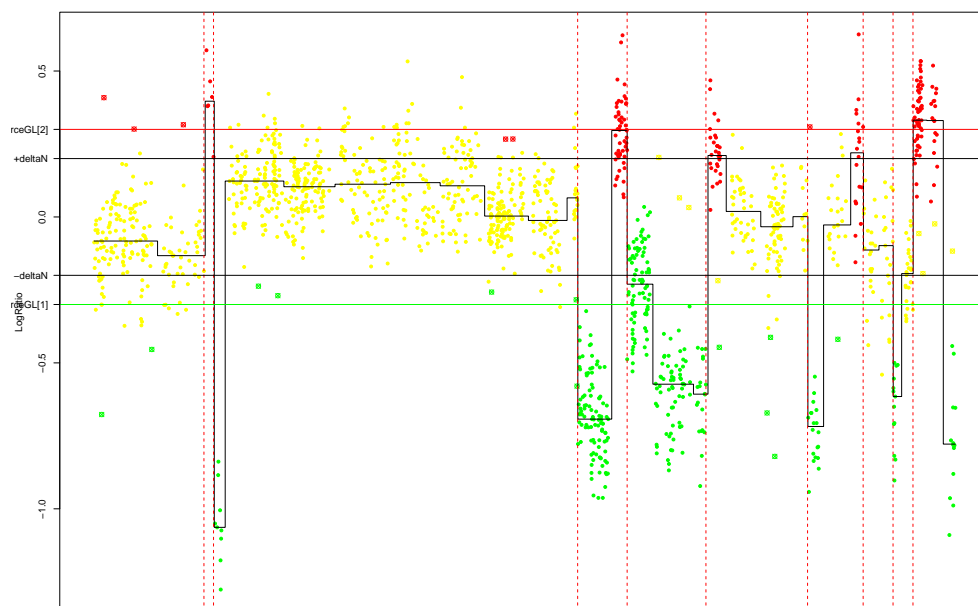


Figure 2: Results of daglad on the patient P9 (Veltman data).

The *daglad* function allows to choose some threshold to help the algorithm to identify the status of the genomic regions. The thresholds are given in the following parameters:

- deltaN
- forceGL
- deletion
- amplicon

Comparing **Figure 2** and **Figure 3** shows the influence of two different sets of parameters.

```

> data(veltman)
> profileCGH <- as.profileCGH(P9)
> profileCGH <- daglad(profileCGH, mediancenter = FALSE, normalrefcenter = FALSE,
+   genomestep = FALSE, smoothfunc = "lawsglad", lkern = "Exponential",

```

```

+     model = "Gaussian", qlambda = 0.999, bandwidth = 10, base = FALSE,
+     round = 1.5, lambdabreak = 8, lambdaclusterGen = 40, param = c(d = 6),
+     alpha = 0.001, msize = 5, method = "centroid", nmin = 1,
+     nmax = 8, amplicon = 1, deletion = -5, deltaN = 0.1, forceGL = c(-0.15,
+     0.15), nbsigma = 3, MinBkpWeight = 0.35, CheckBkpPos = TRUE)

[1] "Smoothing for each Chromosome"
[1] "Optimization of the Breakpoints"
[1] "DNA copy number calling"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.002
[1] "diff"
Time difference of 0.01029611 secs
[1] "hclustglad"
      user system elapsed
0         0         0
[1] "clusterglad"
      user system elapsed
0.188   0.000   0.188
[1] "merge"
      user system elapsed
0.000   0.000   0.001
[1] "zone"
      user system elapsed
0.004   0.000   0.001
[1] "Temps findCluster: 0.437081098556519"
[1] "jointure BkpInfo"
      user system elapsed
0.008   0.000   0.006
[1] "Check Breakpoints Position"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.01035094 secs
[1] "hclustglad"
      user system elapsed
0.000   0.000   0.001
[1] "clusterglad"
      user system elapsed
0.004   0.000   0.000
[1] "merge"
      user system elapsed
0         0         0
[1] "zone"
      user system elapsed
0.004   0.000   0.002
[1] "Temps findCluster: 0.242370128631592"
[1] "subsetdata"

```

```

    user system elapsed
0.000 0.000 0.001
[1] "diff"
Time difference of 0.01046395 secs
[1] "hclustglad"
    user system elapsed
0.000 0.000 0.001
[1] "clusterglad"
    user system elapsed
      0      0      0
[1] "merge"
    user system elapsed
0.000 0.000 0.001
[1] "zone"
    user system elapsed
0.004 0.000 0.001
[1] "Temps findCluster: 0.285469055175781"
[1] "jointure BkpInfo"
    user system elapsed
0.004 0.000 0.005
[1] "subsetdata"
    user system elapsed
0.004 0.000 0.002
[1] "diff"
Time difference of 0.01052809 secs
[1] "hclustglad"
    user system elapsed
0.000 0.000 0.001
[1] "clusterglad"
    user system elapsed
      0      0      0
[1] "merge"
    user system elapsed
0.000 0.000 0.001
[1] "zone"
    user system elapsed
0.004 0.000 0.002
[1] "Temps findCluster: 0.241520881652832"
[1] "subsetdata"
    user system elapsed
0.000 0.000 0.002
[1] "diff"
Time difference of 0.01049113 secs
[1] "hclustglad"
    user system elapsed
      0      0      0
[1] "clusterglad"
    user system elapsed
      0      0      0
[1] "merge"

```

```

      user  system elapsed
      0      0      0
[1] "zone"
      user  system elapsed
0.000 0.000 0.001
[1] "Temps findCluster: 0.240535974502563"
[1] "jointure BkpInfo"
      user  system elapsed
0.004 0.000 0.006
[1] "Results Preparation"

```

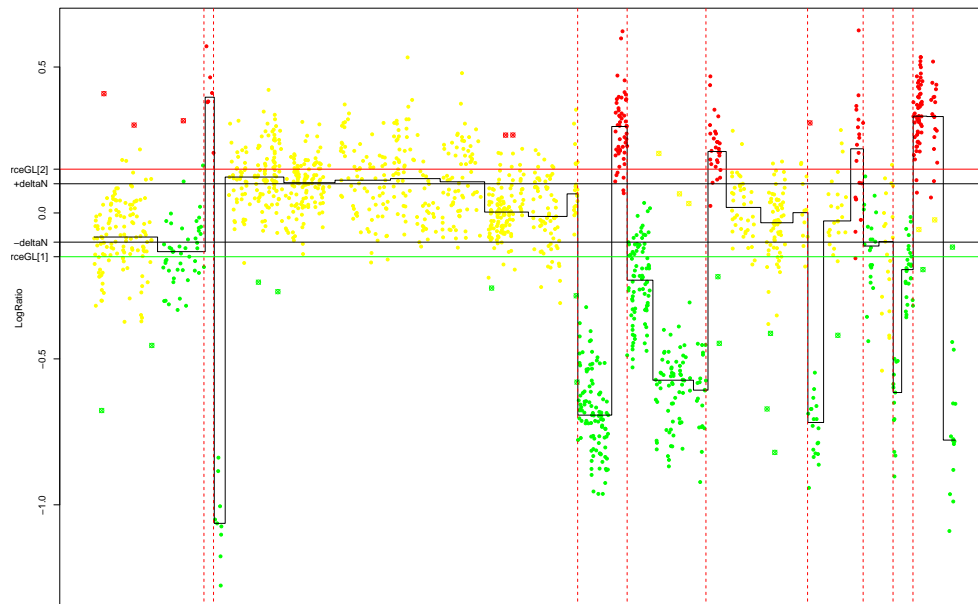


Figure 3: Results of daglad on the patient P9 (Veltman data) - Influence of the thresholds.

The *daglad* function allows a smoothing step over the whole genome (if *genomestep=TRUE*) where all the chromosomes are concatenated together. During this step, the cluster which corresponds to the Normal DNA level is identified: the thresholds used in the function (*deltaN*, *forceGL*, *amplicon*, *deletion*) are then compared to the median of this cluster.

## 4.4 Tuning parameters

The most important parameters are:

- *lambdabreak*
- *lambdacluster*
- *lambdaclusterGen*
- *param*  $c(d = 6)$

Decreasing those parameters will lead to a higher number of breakpoints identified. For arrays experiments with very small Signal to Noise ratio it is recommended to use a small value of *param* like  $d = 3$  or less.

## 5 Graphical functions

### 5.1 Plot of raw array data

```
> data(arrayCGH)
> array <- list(arrayValues = array2, arrayDesign = c(4, 4, 21,
+ 22))
> class(array) <- "arrayCGH"
```

```
> arrayPlot(array, "Log2Rat", bar = "none")
```

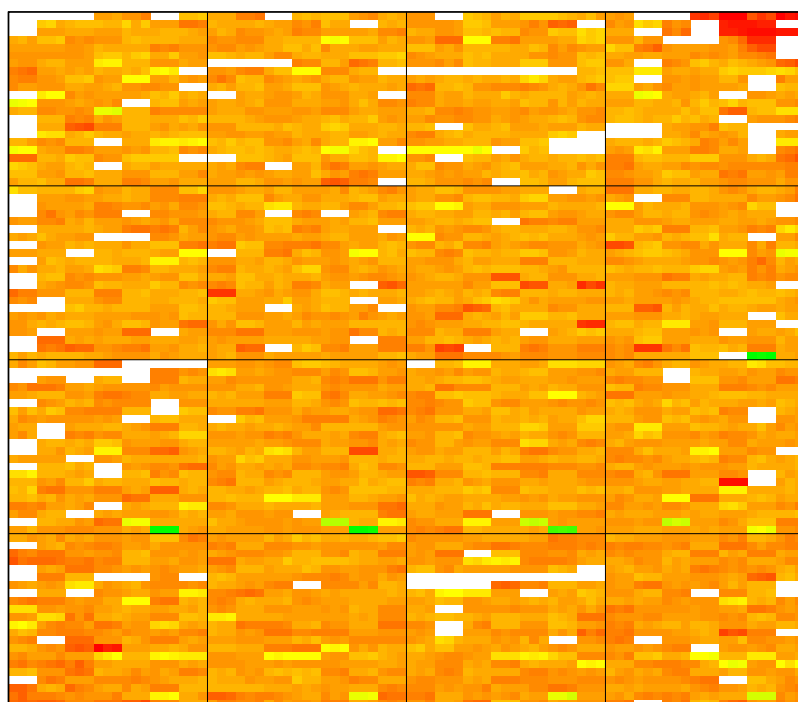


Figure 4: Spatial image of array CGH

```
> arrayPersp(array, "Log2Rat", box = FALSE, theta = 110, phi = 40,  
+           bar = FALSE)
```

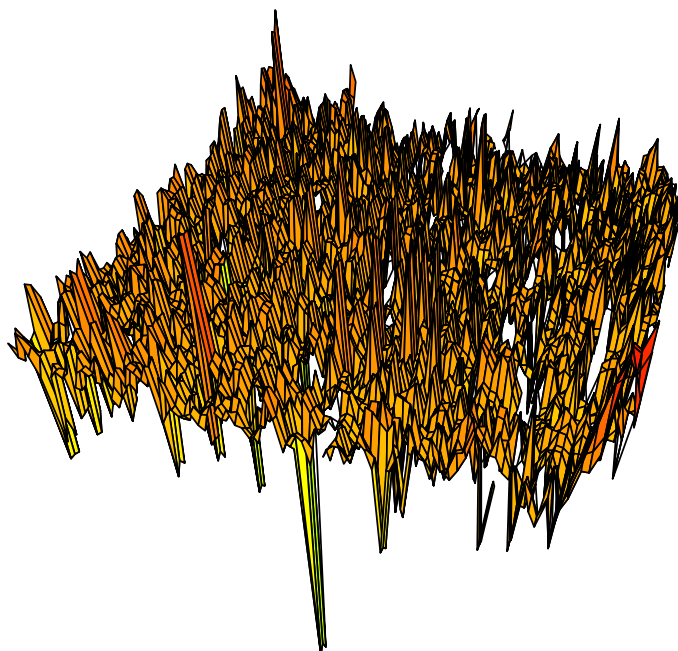


Figure 5: Perspective image of array CGH



## 5.2 Plot of genomic profile

```
[1] "Smoothing for each Chromosome"
[1] "Optimization of the Breakpoints"
[1] "subsetdata"
      user system elapsed
0.000  0.000  0.001
[1] "diff"
Time difference of 0.005570889 secs
[1] "hclustglad"
      user system elapsed
      0      0      0
[1] "clusterglad"
      user system elapsed
0.028  0.000  0.028
[1] "merge"
      user system elapsed
      0      0      0
[1] "Temps findCluster: 0.225516796112061"
[1] "subsetdata"
      user system elapsed
0.000  0.000  0.001
[1] "diff"
Time difference of 0.005251884 secs
[1] "Temps findCluster: 0.0554308891296387"
[1] "subsetdata"
      user system elapsed
0.000  0.000  0.001
[1] "diff"
Time difference of 0.005249977 secs
[1] "Temps findCluster: 0.0552828311920166"
[1] "subsetdata"
      user system elapsed
0.000  0.000  0.001
[1] "diff"
Time difference of 0.005496979 secs
[1] "hclustglad"
      user system elapsed
0.000  0.000  0.001
[1] "clusterglad"
      user system elapsed
0.028  0.000  0.028
[1] "merge"
      user system elapsed
      0      0      0
[1] "Temps findCluster: 0.22668194770813"
[1] "subsetdata"
      user system elapsed
0.000  0.000  0.001
[1] "diff"
```

```

Time difference of 0.005536079 secs
[1] "Temps findCluster: 0.0591039657592773"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005301952 secs
[1] "Temps findCluster: 0.058974027633667"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005347967 secs
[1] "Temps findCluster: 0.0561919212341309"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005339146 secs
[1] "Temps findCluster: 0.0555300712585449"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005337 secs
[1] "Temps findCluster: 0.0597279071807861"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005275965 secs
[1] "Temps findCluster: 0.056098222732544"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.006175995 secs
[1] "hclustglad"
      user system elapsed
0.000   0.000   0.001
[1] "clusterglad"
      user system elapsed
0.088   0.004   0.094
[1] "merge"
      user system elapsed
0.004   0.000   0.000
[1] "Temps findCluster: 0.299787044525146"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001

```

```

[1] "diff"
Time difference of 0.005259037 secs
[1] "Temps findCluster: 0.0594329833984375"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005236149 secs
[1] "Temps findCluster: 0.0556628704071045"
[1] "subsetdata"
      user  system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005250931 secs
[1] "Temps findCluster: 0.055290937423706"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005241156 secs
[1] "Temps findCluster: 0.0554981231689453"
[1] "subsetdata"
      user  system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.005301952 secs
[1] "Temps findCluster: 0.0556838512420654"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005376101 secs
[1] "Temps findCluster: 0.0774569511413574"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005231142 secs
[1] "Temps findCluster: 0.0565159320831299"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005249023 secs
[1] "Temps findCluster: 0.0555820465087891"
[1] "subsetdata"
      user  system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005245924 secs

```

```

[1] "Temps findCluster: 0.0556590557098389"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005246162 secs
[1] "Temps findCluster: 0.0553059577941895"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.001
[1] "diff"
Time difference of 0.005218029 secs
[1] "Temps findCluster: 0.0552899837493896"
[1] "subsetdata"
      user system elapsed
0.004   0.000   0.001
[1] "diff"
Time difference of 0.00525403 secs
[1] "Temps findCluster: 0.0552961826324463"
[1] "subsetdata"
      user system elapsed
0.000   0.000   0.002
[1] "diff"
Time difference of 0.01169491 secs
[1] "hclustglad"
      user system elapsed
0.000   0.000   0.001
[1] "clusterglad"
      user system elapsed
0.188   0.004   0.193
[1] "merge"
      user system elapsed
0.000   0.000   0.001
[1] "zone"
      user system elapsed
0.000   0.000   0.002
[1] "Temps findCluster: 0.462231874465942"
[1] "Results Preparation"

```

```
> plotProfile(res, unit = 3, Bkp = TRUE, labels = FALSE, Smoothing = "Smoothing",
+ plotband = FALSE)
```

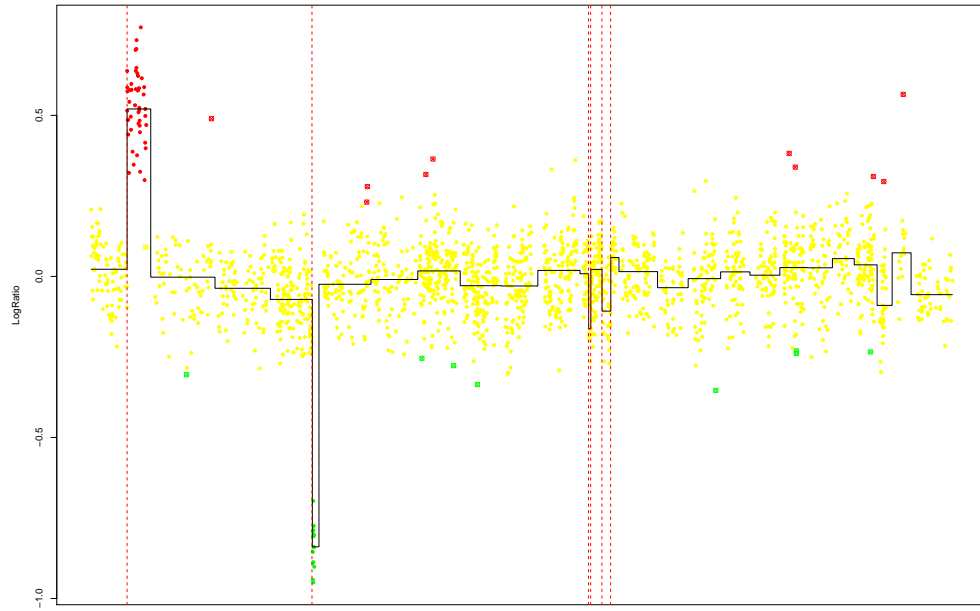


Figure 6: Genomic profile on the whole genome

```
> plotProfile(res, unit = 3, Bkp = TRUE, labels = FALSE, Smoothing = "Smoothing")
```

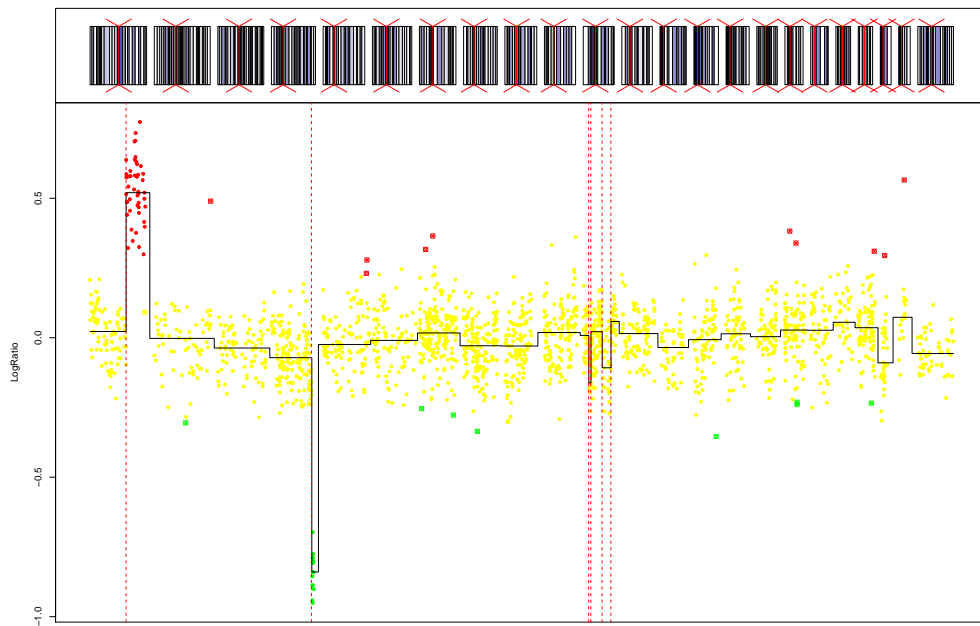


Figure 7: Genomic profile on the whole genome and cytogenetic banding

```

> text <- list(x = c(90000, 2e+05), y = c(0.15, 0.3), labels = c("NORMAL",
+   "GAIN"), cex = 2)
> plotProfile(res, unit = 3, Bkp = TRUE, labels = TRUE, Chromosome = 1,
+   Smoothing = "Smoothing", plotband = FALSE, text = text)

```

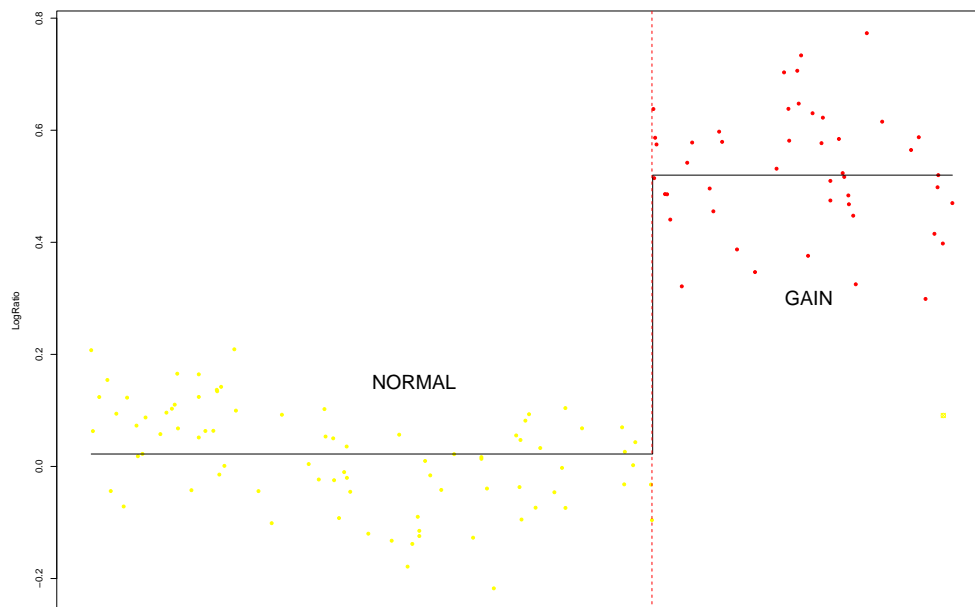


Figure 8: Genomic profile for chromosome 1

```

> text <- list(x = c(90000, 2e+05), y = c(0.15, 0.3), labels = c("NORMAL",
+   "GAIN"), cex = 2)
> plotProfile(res, unit = 3, Bkp = TRUE, labels = TRUE, Chromosome = 1,
+   Smoothing = "Smoothing", text = text, main = "Chromosome 1")

```

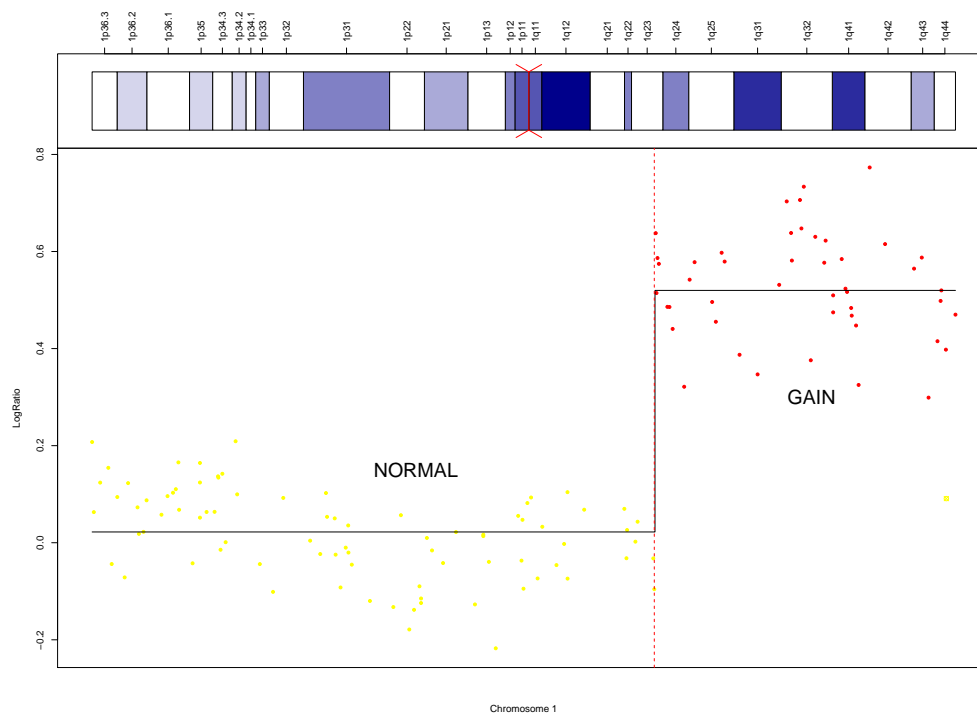


Figure 9: Genomic profile for chromosome 1 and cytogenetic banding with labels

## References

- Ben-Yaacov, E. and Eldar, Y. C. (2008). A fast and flexible method for the segmentation of acgh data. *Bioinformatics*, 24:i139–i145.
- Billerey, C., Chopin, D., Aubriot-Lorton, M. H., Ricol, D., de Medina, S. G. D., Rhijn, B. V., Bralet, M. P., Lefrere-Belda, M. A., Lahaye, J. B., Abbou, C. C., Bonaventure, J., Zafrani, E. S., van der Kwast, T., Thiery, J. P., and Radvanyi, F. (2001). Frequent FGFR3 mutations in papillary non-invasive bladder (pTa) tumors. *Am. J. Pathol.*, 158:955–1959.
- Hupé, P., Stransky, N., Thiery, J. P., Radvanyi, F., and Barillot, E. (2004). Analysis of array CGH data: from signal ratio to gain and loss of DNA regions. *Bioinformatics*, 20:3413–3422.
- Ishkanian, A. S., Malloff, C. A., Watson, S. K., DeLeeuw, R. J., Chi, B., Coe, B. P., Snijders, A., Albertson, D. G., Pinkel, D., Marra, M. A., Ling, V., MacAulay, C., and Lam, W. L. (2004). A tiling resolution DNA microarray with complete coverage of the human genome. *Nat. Genet.*, 36:299–303.
- Pinkel, D., Segreaves, R., Sudar, D., Clark, S., Poole, I., Kowbel, D., Collins, C., Kuo, W. L., Chen, C., Zhai, Y., Dairkee, S. H., Ljung, B. M., Gray, J. W., and Albertson, D. G. (1998). High resolution analysis of dna copy number variation using comparative genomic hybridization to microarrays. *Nat. Genet.*, 20:207–211.
- Polzehl, J. and Spokoiny, S. (2000). Adaptive weights smoothing with applications to image restoration. *J. Roy. Statistical Society, Series B*, pages 335–354.
- Polzehl, J. and Spokoiny, S. (2002). Local likelihood modelling by adaptive weights smoothing. WIAS-Preprint 787.
- Snijders, A. M., Nowak, N., Segreaves, R., Blackwood, S., Brown, N., Conroy, J., Hamilton, G., Hindle, A. K., Huey, B., Kimura, K., S, S. L., Myambo, K., Palmer, J., Ylstra, B., Yue, J. P., Gray, J. W., Jain, A. N., Pinkel, D., and Albertson, D. G. (2001). Assembly of microarrays for genome-wide measurement of dna copy number. *Nat. Genet.*, 29:263–4.
- Solinas-Toldo, S., Lampel, S., Stilgenbauer, S., Nickolenko, J., Benner, A., Dohner, H., Cremer, T., and Lichter, P. (1997). Matrix-based comparative genomic hybridization: Biochips to screen for genomic imbalances. *Genes Chromosomes Cancer*, 20:399–407.
- Veltman, J. A., Fridlyand, J., Pejavar, S., Olshen, A. B., Korkola, J. E., DeVries, S., Carroll, P., Kuo, W.-L., Pinkel, D., Albertson, D., Cordon-Cardo, C., Jain, A. N., and Waldman, F. M. (2003). Array-based comparative genomic hybridization for genome-wide screening of DNA copy number in bladder tumors. *Cancer Res*, 63:2872–2880.